Smallpox

Draft Supplemental Recommendation of the ACIP

Use of Smallpox (Vaccinia) Vaccine, June 2002

Draft approved by ACIP on June 20, 2002
Now Under Consideration by CDC and DHHS

http://www.cdc.gov/nip/smallpox/supp_recs.htm

Introduction

In June 2001, the Advisory Committee on Immunization Practices (ACIP) made recommendations for use of smallpox (vaccinia) vaccine to protect persons working with Orthopoxviruses, to prepare for a possible bioterrorism attack and respond to an attack involving smallpox. Because of the terrorist attacks in the fall of 2001, the Centers for Disease Control and Prevention (CDC) asked the ACIP to review their previous recommendations for smallpox (vaccinia) vaccination. As a result of this review, these supplemental recommendations update those for vaccination of 1) the general population and 2) persons designated to respond or care for a suspected or confirmed case of smallpox. In addition, they clarify and expand the primary strategy for control and containment of smallpox in the event of an outbreak.

Recommendations for vaccination of laboratory workers who directly handle recombinant vaccinia viruses derived from non-highly attenuated vaccinia strains, or other orthopoxviruses that infect humans (e.g., Monkeypox, cowpox, vaccinia, and variola) remain unchanged. Other aspects of the previous recommendations (e.g., screening for contraindications, care of the vaccination site) are being reviewed, and until new recommendations are published, the June 2001 recommendations should be consulted.

Prior to the terrorist attacks in the fall of 2001, the Department of Health and Human Services (DHHS) began to increase public health preparedness through expansion of the existing stockpile of smallpox (vaccinia) vaccine (Dryvax, Wyeth) by purchase of vaccine produced in cell culture (Acambis). The additional purchase of vaccine was initiated to address perceived vulnerability to future terrorist attacks. The anthrax attacks in the fall of 2001 resulted in increased activities to enhance preparedness and response capabilities, including those involving the deliberate release of smallpox and resulted in the accelerated production of additional doses of smallpox (vaccinia) vaccine. This increased supply of vaccine allows for consideration of expanded vaccination options.

The following recommendations were developed after formation of a joint Working Group of the ACIP and the National Vaccine Advisory Committee (NVAC) and a series of public meetings and forums to review available data on smallpox, smallpox (vaccinia) vaccine, smallpox control strategies, and other issues related to smallpox (vaccinia) vaccination. A website was established to solicit public opinion and input on options for smallpox (vaccinia) vaccine use.

The ACIP will review these recommendations periodically, or more urgently if necessary. These reviews will include new information or developments related to smallpox disease, smallpox (vaccinia) vaccines (including vaccine licensure), risk of smallpox attack, smallpox (vaccinia) vaccine adverse events, and the experience gained in the implementation of the current recommendations. Revised recommendations will be developed as needed.

Smallpox Transmission and Control

Smallpox is transmitted from an infected person once a rash appears. Transmission does not occur during the prodromal period that precedes the rash. Infection is transmitted by large droplet nuclei and only rarely has airborne transmission been documented. Epidemiologic studies have shown that smallpox has a lower rate of transmission than diseases such as measles, pertussis, and influenza. The greatest risk of infection occurs among household members and close contacts of persons with smallpox, especially those with prolonged face-to-face exposure. Vaccination and isolation of contacts of cases at greatest risk of infection has been shown to interrupt transmission of smallpox. However, poor infection control practices resulted in high rates of transmission in hospitals.

The primary strategy to control an outbreak of smallpox and interrupt disease transmission is surveillance and containment, which includes ring vaccination and isolation of persons at risk of contracting smallpox. This strategy involves identification of infected persons through intensive surveillance, isolation of infected persons, vaccination of household contacts and other close contacts of infected persons (i.e., primary contacts), and vaccination of household contacts of the primary contacts (i.e. secondary contacts). This strategy was instrumental in the ultimate eradication of smallpox as a naturally occurring disease even in areas that had low vaccination coverage.
Depending upon the size of the smallpox outbreak and the resources that were available for rapid and thorough contact tracing, surveillance and containment activities in areas with identified smallpox cases was sometimes supplemented with voluntary vaccination of other individuals. This was done in order to expand the ring of immune individuals within an outbreak area and to further reduce the chance of secondary transmission from smallpox patients before they could be identified and isolated. Regardless of the geographic distribution, number of cases, or number of concurrent outbreaks, surveillance and containment activities remained the primary disease control strategy.

Critical Considerations

A number of factors and assumptions were used in developing these supplemental recommendations.

- **Level of disease risk and threat**
  Information provided to the ACIP indicated that the risk for smallpox occurring as a

result of a deliberate release by terrorists is considered low, and the population at risk for such an exposure cannot be determined. It was further assumed that regardless of the mode of a bioterrorism release, the epidemiology of subsequent person-to-person transmission would be consistent with prior experience. These recommendations also assumed that in addition to vaccination, health care workers and others would be afforded protection from infection through appropriate infection control measures, including the use of appropriate personal protective equipment.

- **Expected severe adverse reactions to vaccination**
  These supplemental recommendations assume that appropriate screening for contraindications to vaccination would be implemented and would include both the vaccinated persons, as well as their contacts. It is further assumed that recommended precautions would be taken to minimize the risk of adverse events among vaccinees as well as their close contacts (e.g., patients, household members).

- **Vaccine and vaccinia immune globulin (VIG) supply**
  The supplemental recommendations assume that both would be available for use, in sufficient supply, and handled and administered correctly. Smallpox (vaccinia) vaccine and VIG are currently available only under Investigational New Drug (IND) protocols (i.e., protocols for products that are not yet licensed). As such, it was assumed that appropriate informed consent, patient follow-up, and administrative oversight by federal, state, and local public health officials would be required. Further, any administration of smallpox (vaccinia) vaccine would be voluntary.

- **State and local vaccination capacity and capability**
  Surveillance and containment, including ring vaccination, is the primary strategy for the control and containment of smallpox. In addition, state and local health departments would be able, if necessary, to expand immunization to additional groups, up to and including their entire population, in a timely manner.

Smallpox Vaccines and VIG Availability

Currently, there are no commercially available (e.g., licensed) smallpox vaccines. Smallpox vaccines previously produced by Wyeth (Dryvax) and Aventis-Pasteur are available under Investigational New Drug (IND) protocols held by CDC. Both vaccines were prepared from calf lymph with a seed virus derived from the New York City Board of Health strain of vaccinia virus. Studies conducted among young adults with no previous smallpox vaccination history showed that a 1:5 dilution of Dryvax (Wyeth Laboratories, Inc) produced take rates among vaccinees equivalent to those of the undiluted vaccine.

In October 2001, the federal government contracted with Acambis and Acambis-Baxter Pharmaceuticals for at least 209 million doses of smallpox vaccine produced in cell-culture. These vaccines use a clone of the same strain of vaccinia virus (New York City Board of Health), which was utilized in the smallpox vaccines produced from calf lymph. These doses are expected to be available at the end of 2002 or soon thereafter.

Smallpox vaccines are formulated and packaged for administration with a bifurcated needle, which provides a fast, easy, and effective means for administration. All vaccines are packaged in 100 dose vials, except when Dryvax is diluted 1:5 resulting in vials that contain 500 doses.

The CDC National Pharmaceutical Stockpile (NPS) has developed protocols to allow for the rapid, simultaneous delivery of smallpox vaccine to every state and US territory within 12-

24 hours. State and local bioterrorism response plans should provide for the rapid distribution of vaccine within their jurisdiction.
Currently, there is enough VIG available under an IND protocol to treat about 600 serious adverse events. This is enough VIG doses to treat the adverse reactions that would be expected to result from the vaccination of 4 million to 6 million people. Contracts for additional supplies of VIG are in progress.

Surveillance

Currently, cases of febrile rash illnesses, for which smallpox is considered in the differential diagnosis, should be immediately reported to local and/or state health departments. Following evaluation by local/state health departments, if smallpox laboratory diagnostics are considered necessary, the CDC Rash Illness Evaluation Team should be consulted at 770-488-7100 or 404-639-2888. As smallpox was eradicated in 1980 and no longer occurs naturally, an initial case of smallpox must be laboratory confirmed. At this time, laboratory confirmation for smallpox is available only at CDC. Clinical consultation and a preliminary laboratory diagnosis can be completed within 8-24 hours.
To assist medical and public health personnel in evaluating the likelihood of smallpox in patients with febrile rash illnesses, CDC has developed a rash illness assessment algorithm. Poster copies of this algorithm are available from state health departments and on the CDC website Orders for copies of the poster can be made over the Internet at: https://www2.cdc.gov/nchstp_od/PIWeb/niporderform.asp

Surveillance activities, including notification procedures and laboratory confirmation of cases, would change if smallpox is confirmed. Additional information regarding surveillance activities following laboratory confirmation of a smallpox outbreak can be found in the CDC Interim Smallpox Response Plan and Guidelines.

Recommendations

Pre-Release Vaccination of the General Population

Under current circumstances, with no confirmed smallpox, and the risk of an attack assessed as low, vaccination of the general population is not recommended, as the potential benefits of vaccination do not outweigh the risks of vaccine complications.

Recommendations regarding pre-outbreak smallpox vaccination are being made on the basis of an assessment that considers the risks of disease and the benefits and risks of vaccination. The live smallpox (vaccinia) vaccine virus can be transmitted from person to person. In addition to sometimes causing adverse reactions in vaccinated persons, the vaccine virus can cause adverse reactions in the contacts of vaccinated persons. It is assumed that the risk of serious adverse events with currently available vaccines would be similar to those previously observed and could be higher today due to the increased prevalence of persons with altered immune systems.

Pre-Release Vaccination of Selected Groups to Enhance Smallpox Response Readiness

Smallpox Response Teams

Smallpox vaccination is recommended for persons pre-designated by the appropriate bioterrorism and public health authorities to conduct investigation and follow-up of initial smallpox cases that would necessitate direct patient contact.

To enhance public health preparedness and response for smallpox control, specific teams at the federal, state and local level should be established to investigate and facilitate the diagnostic work-up of the initial suspect case(s) of smallpox and initiate control measures. These Smallpox Response Teams might include persons designated as medical team leader, public health advisor, medical epidemiologists, disease investigators, diagnostic laboratory scientist, nurses, personnel who would administer smallpox vaccines, and security/law enforcement personnel. Such teams may also include medical personnel who would assist in the evaluation of suspected smallpox cases.

The ACIP recommends that each state and territory establish and maintain at least one Smallpox Response Team. Considerations for additional teams should take into account population and geographic considerations and should be developed in accordance with federal, state, and local bioterrorism plans.

Designated Smallpox Healthcare Personnel at Designated Hospitals

Smallpox vaccination is recommended for selected personnel in facilities pre-designated to serve as referral centers to provide care for the initial cases of smallpox. These facilities would be pre-designated by the appropriate bioterrorism and public health authorities, and personnel within these facilities would be designated by the hospital.

As outlined in the CDC Interim Smallpox Response Plan and Guidelines, state bioterrorism response plans should designate initial smallpox isolation and care facilities (e.g., type C facilities). In turn, these facilities should pre-designate individuals who would care for the initial smallpox cases. To staff augmented medical response capabilities, additional personnel should be identified and trained to care for smallpox patients.

Implementation of Recommendations

The ACIP recognizes that the implementation of the supplemental recommendations presented in this document requires addressing a number of issues, and that this will take time. The issues include provider and public education, health care provider training, availability of vaccine and VIG, developing the appropriate investigational new drug protocols, screening, strategies to minimize vaccine wastage, vaccine adverse event surveillance, and other logistical and administrative issues.